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| 10/501,032 | 01/06/2006 | Anne Lunden | 17917-002US1 | 1762 |

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EXAMINER

MEAH, MOHAMMAD Y

| ART UNIT | PAPER NUMBER |
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1652

DATE MAILED: 10/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/501,032

Applicant(s)

LUNDEN ET AL.

Examiner

Mohammad Meah

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 10-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 443/05
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

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DETAILED ACTION

With preliminary amendment of this application, the applicant, on date 07/28/2006 elected without traverse Group III (claims 10-16) for examination.

Election/Restriction

During preliminary amendment of this application, the applicant, on date 07/28/2006 elected without traverse Group III (claims 10 -16), drawn to a method of detecting mutation in FMO3 gene in mammal using a polynucleotide encoding a FMO3 polypeptide of SEQ ID NO: 15, for examination. Groups I-II and (claims 2-3, 18-21) of election/restriction-office action of date 06/07/2005 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Priority

Acknowledgement is made of applicant's priority date based on application filing date of 1/09/2003 for PCT/IBO3/00028 and filing date 01/09/2002 for foreign application PA200200031 filed in Denmark Japan: Application No. Japan 2002-293512.

Objections

Claim 10~~6~~ is objected because it is dependent on non-elected claims. Appropriate correction is required.

Claim Rejections

35 U.S.C 112

Claims 10,15-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10,15-16 are indefinite in the recitation of "stringent conditions" as the specification does not define what conditions constitute "stringent". While page 6 of the specification describes some conditions, which are intended to be stringent, there is nothing to suggest that other conditions would not also be included within the scope of this term and in the art what is considered stringent varies widely depending on the individual situation as well as the person making the determination. As such it is unclear how homologous to the sequence of a gene encoding SEQ ID NO: 15, a sequence must be to be included within the scope of these claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to method of detecting any mutated FMO3 gene in any mammal that cause lack of trimethyl amine metabolism by using a genus of DNA probe or primer molecules encoding any mutated protein having FMO3 activity from any source. The specification teaches the structure of only one representative mutated FMO3 DNA that cause lack of trimethyl amine metabolism in cattle and a few polynucleotides probes for detecting such mutated genes. Although, the specification sets forth sufficient identifying characteristics of this specific FMO3 polymorphism (i.e., complete sequence of the cattle FMO3 gene and specific mutation that cause lack of trimethyl amine metabolism) it does not sufficiently describe any mutation of any FMO3 gene that can cause lack of trimethyl amine metabolism and as well as whether the same mutation can cause lack of trimethyl amine metabolism in any mammal. Not every mutation of a gene produces similar functional effects on the protein and the specification provides no disclosure of other mutations of FMO3 genes which result in alteration in trimethyl amine metabolism. Therefore how to detect any mutation which causes an alteration in trimethyl amine metabolism in any mammal using any probe or primer of any FMO3 gene is not sufficiently described. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 10-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of detecting R238X mutation of

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FMO3 of SEQ ID NO: 15 of a bovine that cause lack of trimethyl amine metabolism using a FMO3 DNA probe of SEQ ID NO: 10 does not reasonably provide enablement for detecting any mutation of any FMO3 protein in any mammal or any mutation of a FMO3 encoded by any DNA which hybridize in any stringent condition with SEQ ID NO: 14 or any DNA which encode any protein having 85% identity with SEQ ID NO:15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 10-16 are so broad as to encompass any method of detecting any mutation of any FMO3 protein which cause lack of trimethyl amine metabolism in any mammal or any mutation of a FMO3 that cause lack of trimethyl amine metabolism encoded by any DNA which hybridize in any stringent condition with SEQ ID NO: 14 or any DNA which encode any protein having 85% identity with SEQ ID NO:15 and cause lack of trimethyl amine metabolism. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number mutations of FMO3 which may or may not correlate to lack of trimethyl amine metabolism and large number of methods of detecting them. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which mutations of a protein sequence will produce a specific functional modification requires a detailed knowledge of the ways in which the protein's structure relates to its function. Furthermore, merely because one or more alterations of a particular protein could cause an expected effect does not indicate whether these alterations actually occur in vivo in one or more mammals and many polymorphisms in mammals have no

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functional effect on the protein at all. Therefore a skilled artisan would not be able to predict clearly from the presence of a change in one or more FMO3 genes whether that change would produce an alteration trimethyl amine metabolism or not. However, in this case the disclosure is limited to the mutation of R238X mutation of FMO3 polypeptide of SEQ ID NO: 14.

The specification does not support the broad scope of the claims which encompass detecting any mutation of any FMO3 protein which cause lack of trimethyl amine metabolism in any mammal or any mutation of any FMO3 which cause lack of trimethyl amine metabolism encoded by any DNA which hybridize in any stringent condition with SEQ ID NO: 14 or any DNA which encode any protein having 85% identity with SEQ ID NO:15 because the specification does **not** establish: (A) regions of the DNA structure which correlates to alterations in trimethyl amine metabolism activity; (B) the presence or absence of similar variants in any mammalian FMO3 gene; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims to broadly detecting any mutation of any FMO3 protein which cause lack of trimethyl amine metabolism in any mammal or any mutation of a FMO3 which cause lack of trimethyl amine metabolism encoded by any DNA which hybridize in any stringent condition with SEQ ID NO: 14 or with any DNA which encode any protein having 85% identity with SEQ ID NO:15 The scope of the claims

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must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of FMO3 gene, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

CLAIM Rejection - 35 U.S.C 102

35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Treacy et al. (WO 01/23603, 09/28/2000).

Treacy et al. teach method of detecting FMO3 gene mutation in mammalian FMO3 gene (A52T and R387L) that cause trimethylaminuria by detecting mutations of FMO3 gene or polymorphic variants of FMO3 gene using DNA

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Primers of SEQ ID NO: 1 or 2 from the mammal and amplifying by PCR and the detecting said amplified DNA.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

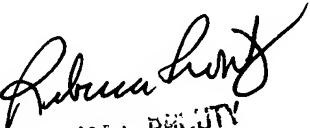
Mohammad Younus Meah, PhD

Examiner, Art Unit 1652

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